Early Biochemical Relapse After Radical Prostatectomy: Which Prostate Cancer Patients May Benefit from a Restaging ^{11}C-Choline PET/CT Scan Before Salvage Radiation Therapy?

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The aim of the study was to assess which factors may influence ^{11}C-choline PET/CT detection rate in a population of recurrent prostate cancer (PCa) patients listed for salvage radiation therapy (S-RT) in an early phase of biochemical relapse, to select which patients could obtain the most benefit by performing restaging ^{11}C-choline PET/CT before S-RT. **Methods:** The study comprised 605 patients, treated with radical prostatectomy (RP) with curative intent for PCa who showed rising PSA levels after primary therapy and listed for S-RT. Prostate-specific antigen (PSA) values were >0.2 ng/mL and <2 ng/mL (mean, 1.05 ng/mL; median, 1.07 ng/mL; range, 0.2–2 ng/m; SD, ±0.59). All patients were classified as N0 after RP. Seventeen of 605 patients received adjuvant RT together with RP, whereas 148 of 605 patients received androgen-deprivation therapy (ADT) at the time of PET/CT. PSA, PSA kinetics, Gleason score, age, time to biochemical relapse, ADT, and initial tumor stage were statistically analyzed to assess which factor could influence PET/CT positivity and the detection of local versus distant relapse. **Results:** ^{11}C-choline PET/CT was positive in 28.4% of patients (172/605). Eighty-three of 605 patients were positive in the pelvis (group A), distant metastasis (group B) were detected in 72 of 605 patients, and local and distant sites of relapse were detected in 17 of 605 patients (group C). At multivariate analysis, PSA, PSA doubling time (PSAdt), and ongoing ADT were significant predictors for positive scan results, whereas PSA and PSAdt were significantly related to distant relapse detection ($P < 0.05$). At the receiver-operating-characteristic analysis, a PSA value of 1.05 ng/mL and PSAdt of 5.95 mo were determined to be the optimal cutoff values in the prediction of a positive ^{11}C-choline PET/CT scan, with an area under the curve (AUC) of 0.625 for PSA and 0.677 for PSAdt. **Conclusion:** ^{11}C-choline PET/CT may be suggested before S-RT during the early phase of biochemical relapse, to select patients who may benefit from this aggressive treatment. Particularly, patients showing fast PSA kinetics or PSA increasing levels despite ongoing ADT should be studied with ^{11}C-choline PET/CT before S-RT, considering the higher probability to detect positive findings outside the pelvis.

Key Words: ^{11}C-choline PET/CT; prostate cancer; biochemical relapse; PSA kinetics; risk factors

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Prostate cancer (PCa) is the third cause of cancer-related death in developed countries (*1*). Serum levels of prostate-specific antigen (PSA), digital rectal examination, and transrectal ultrasound (TRUS)–guided biopsies are usually performed to diagnose and locally stage the disease (*2*). Primary treatment depends on age, local and distant staging, surgical risk, and performance status. The most common approaches include radical prostatectomy (RP), external-beam radiation therapy (EBRT), brachytherapy (alone or in combination with EBRT), and androgen-deprivation therapy (ADT) with adjuvant intent (*2*). PSA value is the most reliable and cost-effective biomarker of biochemical relapse (BR) during patient follow-up after primary treatment. BR occurs in up to 50% of patients and is defined as an increase of serum PSA level (PSA > 0.2 ng/mL after RP or >2 ng/mL after EBRT (*3,4*)). In the case of BR, it is crucial for therapeutic decision making to determine the real site and the exact number of tumor recurrences. BR is associated with the presence of prostate bed recurrences, metastatic spread to locoregional pelvic lymph nodes (LNs), or distant metastases. Imaging has a limited role in the detection of the site of recurrence, with bone scintigraphy or CT that may show the site of relapse only if PSA reaches very high levels (>20 ng/mL) or in the case of fast PSA kinetics (*5,6*). TRUS-guided biopsy also showed a limited sensitivity (*7*) to detect local relapses, and a negative biopsy cannot exclude the presence of local relapse. For this purpose, MR imaging recently showed better results (*8*). Prostatic bed relapse without evidence of locoregional LN involvement or distant metastases is usually suitable for salvage radiotherapy (S-RT) (*9*). It has been established that the outcome of the patient who received S-RT is optimized when PSA level is as low as reasonably possible (*10,11*), and there is a direct relation between patient outcome and PSA or PSA kinetics values at the moment of S-RT (*10*). Conversely, patients in whom distant metastases or locoregional LN involvement is suspected may not benefit from S-RT: they are usually treated with ADT regardless of the site of recurrence. Recently, it was suggested that aggressive therapeutic approaches in

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PCa patients with proven distant recurrence could be feasible and increase the biochemical free survival (*12–14*). PET/CT using ^{11}C- or ^{18}F-labeled choline may have a role in this scenario (*15*). ^{18}F-FDG PET/CT has shown limited value in this field, whereas it seems that ^{11}C- or ^{18}F-labeled choline may provide similar results (*15*); however, studies designed to compare ^{11}C- or ^{18}F-choline feasibility in similar patient populations have not been performed yet. ^{11}C-choline PET/CT may show the site of tumor recurrence earlier than other imaging methods, in a single-step examination, and its detection rate is directly related to PSA values and PSA kinetics (*16–19*). However, there are no precise indications about the proper use of this tool during BR. Most of the studies published so far have evaluated populations composed of patients showing BR after RP or EBRT, even at the first BR after primary treatment or after systemic therapies during BR (*15*). The heterogeneity of these selected populations could be one of the factors that hindered a proper understanding of the potential role of ^{11}C-choline PET/CT imaging in recurrent PCa patients. For these reasons, different aspects in the ^{11}C-choline PET/CT management of this population, such as different risk factors, optimal timing, and clinical impact on secondary therapy management, have yet to be clarified.

The aim of the study was to retrospectively evaluate the usefulness of ^{11}C-choline PET/CT in recurrent PCa patients listed for S-RT in an early phase of BR through a large population. A statistical analysis of risk factors influencing ^{11}C-choline PET/CT detection rate was performed to select which patients could get the most benefit by performing ^{11}C-choline PET/CT before S-RT.

MATERIALS AND METHODS

Patient Population

This retrospective study was performed according to the declaration of Helsinki, to National regulations, and to local committee recommendations. All patients gave general permission for the use of their clinical data for scientific purposes and informed consent for the anonymous publication of data. We analyzed all clinical records of patients referred to our center from 2008 to January 2013 for recurrent PCa. Inclusion criteria were RP with curative intent for PCa as primary treatment, with or without adjuvant RT; biochemical relapse (rising PSA levels $>$ 0.2 ng/mL and $<$2 ng/mL); all patients classified as N0 after RP; patients already listed for S-RT; and no S-RT previously performed during BR. We retrospectively enrolled 605 patients who matched all the inclusion criteria. This population constitutes an original set of patients not enrolled in previous studies. Population characteristics are shown in Table 1.

Radiopharmaceuticals and Imaging Protocols

^{11}C-choline was synthesized according to the solid-phase method as described by Pascali et al. (*20*) as reported in our previous publications (*19,21,22*). Patients underwent ^{11}C-choline PET/CT following the standard procedure in our center. All scans were obtained with a PET/CT scanner (Discovery LS and Discovery STE; GE Healthcare). CT parameters were 120 kVp, 60 mA, 0.8 s per tube rotation, slice thickness of 5 mm, pitch of 1.5, and a table speed of 30 mm/rotation. Patients received an intravenous injection of 370–555 MBq of ^{11}C-choline, and the PET/CT scan started 3–5 min after radiotracer injection. Emission data were acquired for 5–6 bed positions from the mid thigh to the base of the skull, taking 3–4 min for each bed position.

Image Analysis and Validation Criteria

All ^{11}C-choline PET/CT images were analyzed with dedicated software (eNTEGRA; GE Healthcare), which allowed the review of PET, CT, and fused imaging data. PET images were first assessed visually and interpreted, by consensus, by 2 experienced nuclear medicine physicians aware of the clinical data. Visual interpretation was the main criterion to reach the final diagnosis. Any uptake higher than background was considered as possible malignancy. The maximum standardized uptake value (SUV_{max}) was measured for each lesion, but it was not used as a main criterion to reach the final diagnosis, because a real cutoff has not been established yet. Disagreements between readers were found in only 2% (13/605) of ^{11}C-choline PET/CT images. The final diagnosis was reached by consensus and by the opinion of a third reader.

^{11}C-choline PET/CT–positive findings were validated by TRUS-guided biopsy in the case of local recurrence in 116 of 605 (19.1%) patients and by clinical follow-up lasting more than 12 mo in 518 of 605 (81.9%) patients using contrast-enhanced CT, MR imaging, bone scintigraphy, or repeated ^{11}C-choline PET/CT, which revealed the appearance of further metastatic lesions or the disappearance of metastatic lesions with a normalization of PSA values (PSA $<$ 0.2 ng/mL) after therapies.

Statistical Risk Factor Analysis

All data reported in this work were expressed as mean, median, range, and SD for each value. PSA kinetics were calculated according to Khan et al. (*23*). *t* test and ANOVA were used to compare continuous variables. The χ^2 test was used for categoric variables. At the univariate and multivariate binary logistic analysis, trigger PSA levels, PSA doubling time (PSAdt), and PSA velocity (PSAvel) were coded as continuous variables; Gleason score (GS) (grouped as $<$7 vs. $\geq$7), tumor stage (grouped as $<$T3 vs. $\geq$T3), ongoing ADT (yes vs. no), and age ($<$65 vs. $\geq$65 y) were coded as categoric variables. The receiver-operating-characteristic (ROC) curve was generated by plotting sensitivity versus 1 − specificity and was assessed to find the best cutoff point for PSA and PSAdt to predict a positive ^{11}C-choline PET/CT. The association between clinical and pathologic features and ^{11}C-choline PET/CT findings was assessed using univariate and multivariate binary logistic analysis. The odds ratio (OR) computed by the logistic regression, together with their 95% confidence intervals (CIs), were reported. The regression coefficients of each variable were also provided. The Hosmer–Lemeshow test was used to assess the goodness of fit in the multivariate analysis. All tests were 2-sided. Statistical significance was taken at a *P* value of less than 0.05. All statistical analyses were performed using the SPSS statistical software package (version 21; SPSS Inc.).

RESULTS

^{11}C-choline PET/CT was positive in 172 of 605 patients, with a detection rate of 28.4%. Eighty-three patients (group A) were positive in the pelvis (prostate bed or iliac LNs or pararectal LNs): 33 of 83 showed prostate bed relapse, 4 of 83 prostate bed and locoregional LNs, and 46 of 83 locoregional LNs (Fig. 1). Seventy-four patients (group B) were positive outside the pelvis (distant LNs or retroperitoneal LNs or bone lesions): 23 of 74 distant or retroperitoneal LNs, 47 of 74 bone lesions, and 4 of 74 bone and LNs. Fifteen patients (group C) showed local and distant findings: 9 of 15 locoregional and distant LNs; 3 of 17 locoregional LNs and bone lesions; 1 of 17 prostate bed and bone; 1 of 17 local relapse, locoregional LNs, and distant LNs; and 1 of 17 locoregional LNs, distant LNs, and bone (Fig. 2). ^{11}C-choline PET/CT detected distant (extrapelvic) lesions in 14.8% (89/605) of patients listed for an S-RT in the prostatic bed. Moreover, in 8.3% (50/605) of patients, locoregional LNs (with or without prostate bed involvement) were detected.

SUV_{max} of positive findings ranged from 2.1 to 6.7 in the case of local deposit, from 1.8 to 7.3 in the case of LN deposit, and from 1.5 to 18.9 in the case of bone deposit. No statistical difference

TABLE 1
Population Characteristics

Characteristic	Mean	Median ± SD	Range	Frequency	%
Age (y)	68.9	70 ± 6.7	47–84		
PSA (ng/mL)	1	1.1 ± 0.6	0.2–2		
PSAdt (mo)	8.5	6 ± 8.6	0.3–48		
PSAVel (ng/mL/y)	8.2	3.7 ± 1.7	0.1–15.6		
GS	Median, 7		4–9		
TNM	T2cN0M0		T2aN0M0, T4N0M0		
Primary therapies					
RP				487	80.5
RP + adjuvant RT				118	19.5
Ongoing ADT				148	24.5
Time to relapse (mo)					
<12			19.2	116	
>12			80.8	489	

n = 605 patients.

was observed between mean values of SUV_{max} among different groups ($P > 0.05$).

Results for PSA values and PSA kinetics in PET-positive and PET-negative patients are shown in Table 2. *t* test and ANOVA showed significant differences in PSA and PSA kinetics between ^{11}C-choline PET/CT–positive and ^{11}C-choline PET/CT–negative patients (PSA $P < 0.001$; PSAdt $P < 0.001$; PSAvel $P < 0.001$). Binary logistic regression analyses are shown in Table 3. Multivariate analysis resulted only in PSA, PSAdt, and ongoing ADT as statistical significant predictors for a positive scan. Univariate and multivariate binary logistic regression analysis for detection of distant relapse (paraaortic or retroperitoneal LNs or bone lesions) resulted in PSA (OR, 2.143; 95% CI, 1.190–3.859; $P = 0.011$) and PSAdt (OR, 0.791; 95% CI, 0.705–0.886; $P < 0.001$) as significant predictors. At ROC analysis, a PSA of 1.05 ng/mL and PSAdt of 5.95 mo resulted in an optimal cutoff value in the prediction of a positive ^{11}C-choline PET/CT finding, with an area under the curve (AUC) of 0.625 for PSA and 0.677 for PSAdt.

Twenty-three patients demonstrated false-negative findings for local relapse at histologic analysis. Fourteen of 23 patients were previously treated with adjuvant RT after RP.

According to predictive risk factors that proved to be statistically significant at multivariate analysis for the detection of distant relapse (PSA and PSAdt), we divided our population into 2 different subpopulations according to ROC analysis cutoff values for PSA (1.05 ng/mL) and PSAdt (5.95 mo). In a subpopulation of 139 patients showing a PSA > 1.05 ng/mL (PSA range, 0.2–1.05 ng/mL) and PSAdt ≥ 5.95 mo, PET/CT was positive in 7.9% (11/139) and in 3.6% (5/139) showed bone metastasis; in 2.1% (3/139) PET/CT showed positive locoregional LNs. In a subpopulation of 185 patients with a PSA ≥ 1 (PSA range, 1.05–2 ng/mL) and PSAdt < 5.95 mo, PET/CT was positive in 48.6% (90/185) of patients and in 28.6% (53/185) showed the presence of distant relapse (group B and group C), whereas in 9.8% (18/185) of patients ^{11}C-choline PET/CT detected locoregional LNs.

Considering that ongoing ADT proved to be a significant statistical predictor of a positive ^{11}C-choline PET/CT scan together with PSA and PSAdt, we divided the population into an additional 2 subpopulations, taking into consideration these 3 factors. In a subpopulation of 129 patients showing a PSA < 1.05 ng/mL (PSA range, 0.2–1.05 ng/mL) and PSAdt ≥ 5.95 mo and who did not receive ADT, ^{11}C-choline PET/CT was positive in 4.6% (6/129) of patients and showed bone metastasis in 2.3% (3/129) of patients, whereas in 1.5% (2/129) of patients ^{11}C-choline PET/CT detected positive locoregional LNs. In a subpopulation of 68 patients with a PSA ≥ 1.05 ng/mL (PSA range, 1.05–2 ng/mL) and PSAdt < 5.95 mo and treated with ADT at the time of the scan, ^{11}C-choline PET/CT was positive in 61.8% (42/68) of patients and in 36.8% (25/68) of patients showed distant relapse (group B and group C), whereas in 17.6% (12/68) of patients ^{11}C-choline PET/CT detected positive locoregional LNs. All these results, together with an analysis of each single risk factor assessed, are shown in Table 4 and Figure 3.

In 78 patients, we collected complete clinical follow-up information in a period ranging from 24 to 56 mo: 27 of 42 (64.2%) ^{11}C-choline PET/CT–positive patients relapsed after secondary therapies, and in 15 of 42 patients (35.8%) PSA was not dosable at the end of follow-up. All 15 patients were treated with PET-guided salvage therapies (14 S-RT and 1 salvage-pelvic lymph node dissection). Twenty-six of thirty-six ^{11}C-choline PET/CT–negative patients were treated with S-RT on the prostate bed as scheduled before ^{11}C-choline PET/CT. In 16 of 26 patients (61.2%), PSA was not dosable at the end of follow-up, and 10 of 26 patients (38.8%) showed biochemical relapse.

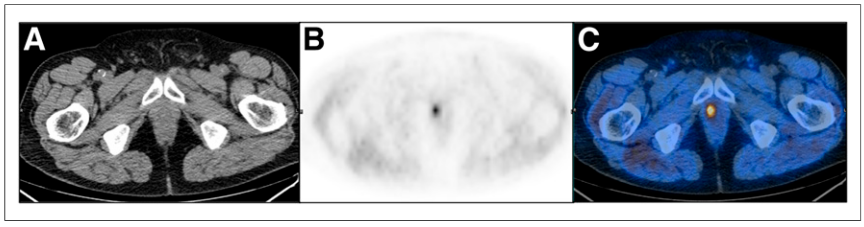

FIGURE 1. A 68-y-old patient treated with RP for PCa (T3aN0M0; GS = 4 + 4). PSA = 0.85 ng/mL, PSAdt = 7.4 mo, PSAvel = 0.94 ng/mL/y. ^{11}C-choline PET/CT showed a positive finding in prostate bed, later confirmed at histologic analysis. (A) CT image. (B) PET image. (C) Fusion image.

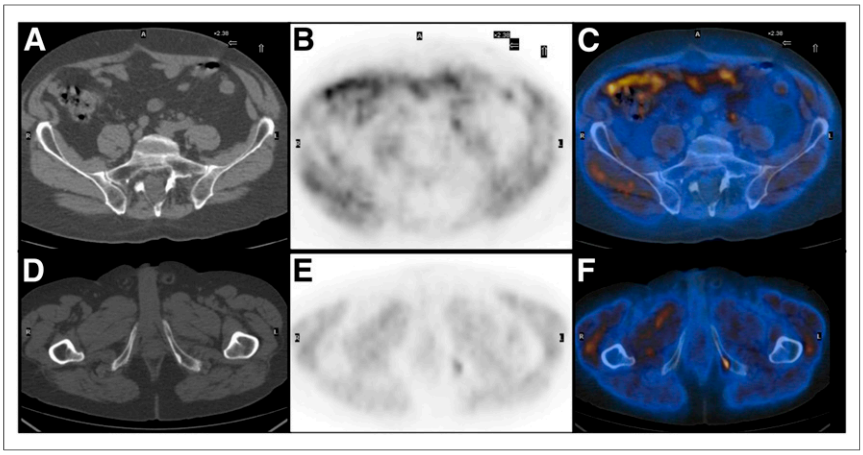

FIGURE 2. A 76-y-old patient treated with RP for PCa (T2bN0M0; GS = 4 + 3). PSA = 1.95 ng/mL, PSAdt = 4.8 mo, PSAvel = 1.6 ng/mL/y. Patient was scheduled for S-RT. ^{11}C-choline PET/CT performed before S-RT (Fig. 1A) showed pathologic choline uptake in common subcentimetric right iliac LN (CT [A], PET [B], and fusion [C] images) and small solitary bone lesion on left ischium (CT [D], PET [E], and fusion [F] images).

DISCUSSION

Detecting extrapelvic relapses in the early phase of BR after RP is still a major issue for clinicians. At the present time, none of the main international guidelines recommend any imaging procedure if there is no evidence of a clinically detectable lesion treatable with palliative intent or PSA does not reach very high levels (PSA > 20 ng/mL) (*2,3,24*). On the basis of tumor and node status, GS, PSA values, PSA kinetics, time to biochemical relapse, many risk tables, and predictive nomograms have been generated to help clinicians in the detection of the site of recurrence (local vs. distant) (*25*). Despite a relatively high sensitivity, a common drawback of nomograms is that they do not show the exact site and number of recurrences. After radical prostatectomy as primary treatment, a relevant distinction should be made between salvage therapies with curative intent (S-RT, tomotherapy, pelvic or retroperitoneal LN dissection) and therapies with palliative intent (ADT, bisphosphonates, bone pain palliative RT). At the present time, in the case of early relapse and low PSA values (*10,11*) patients are treated with S-RT in the prostatic bed with or without diagnostic or histologic confirmation of local relapse (*25,26*). For the best chance of success, S-RT should be administered when the serum PSA first reaches detectable levels, with the purpose being to treat a disease still confined to the pelvis (*10,11,27*). In a study designed by Stephenson et al. (*10*), it was reported that an estimated 48% of patients who received S-RT alone at PSA levels of 0.50 ng/mL or less were free of progression at 6 y, compared with 26% for those treated at higher PSA levels. However, most patients treated with S-RT showed BR after salvage treatments. For this reason, also at the early phase of BR, all efforts should be attempted to exclude the presence of distant metastasis, outside of those included in the field of treatment. Accordingly, the presence of additional lesions, other than those treated with radical intent in the prostatic bed, will make ineffective any targeted therapy. Current diagnostic modalities proved to be inadequate to select patients for S-RT, despite the fact that ^{11}C-choline PET/CT showed a better accuracy than conventional imaging in recurrent PCa patients, especially in the case of low PSA values (*5,6,28*). Considering that ^{11}C-choline PET/CT is still an expensive and not widely available imaging procedure, the use of ^{11}C-choline PET/CT should be optimized, and a careful selection of patients who may potentially benefit from restaging ^{11}C-choline PET/CT before S-RT is necessary.

In the current study, only patients in an early phase of BR (PSA < 2 ng/mL) and already listed for S-RT on the prostate bed have been enrolled. In our series, radiation oncologists decided to not perform S-RT in the patients showing distant choline uptake, despite the lack of a histologic gold standard. Furthermore, in a smaller proportion of the whole population, 8.3% (50/605) of patients, ^{11}C-choline PET/CT showed the presence of locoregional LNs. In this context, the S-RT on the prostate bed intended before ^{11}C-choline PET/CT has been performed in an extended planning target volume including ^{11}C-choline PET/CT–positive findings (*29*).

We identified the characteristics of patients in which ^{11}C-choline PET/CT showed deposits outside the prostate bed. Table 4 shows patient subpopulations grouped according to the risk factors that proved to be significant predictors of ^{11}C-choline PET/CT positivity (PSA, PSAdt, and ongoing ADT) and for the detection of a distant site of relapse (PSA and PSAdt). According to cutoff values suggested by the ROC curve analysis (PSA, 1.05 ng/mL, and PSAdt, 5.95 mo), there is a significant difference in the detection rate of distant lesions in the 2 subpopulations of high-risk and low-risk patients (P < 0,05). Moreover, if we select an additional subpopulation of patients with ongoing ADT at the time of ^{11}C-choline PET/CT (castrate-resistant patients), we also observe a significant proportion of positive findings (regardless of PSA or PSA kinetics). In fact, as recently reported (*21*), the ^{11}C-choline PET/CT detection rate is higher in castrate-resistant patients showing rising PSA values during ADT. Finally, when patients with very high risk of distant relapse (PSA ≥ 1.05 ng/mL; range, 1.05–2 ng/mL; PSAdt < 5.95; ongoing ADT) were grouped together, ^{11}C-choline PET/CT showed positive findings in 61.8% of patients and showed the presence of extrapelvic focal uptake in 38.6%. Conversely, when patients with very low risk of distant relapse (PSA < 1.05 ng/mL; PSAdt ≥ 5.95; no ongoing ADT) were grouped together, ^{11}C-choline PET/CT was positive in 4.6% of patients and detected distant deposit in a restricted percentage of patients (2.3%). Findings of

TABLE 2
PSA Values and PSA Kinetics in PET-Positive and PET-Negative Patients

Patient	Frequency	%	Mean	Median ± SD	Range
PET-positive	172	28.4			
PSA			1.3	1.2 ± 0.5	0.2–2
PSAdt			4.6	3.8 ± 0.3	0.7–21
PSAvel			2.2	1.6 ± 2.1	0.1–15.6
PET-negative	433	71.6			
PSA			1.0	1.1 ± 0.5	0.2–2
PSAdt			10.3	7.3 ± 9.7	0.4–48.0
PSAvel			1.1	0.6 ± 1.4	0.1–9.9

TABLE 3
Univariate and Multivariate Binary Logistic Regression Analysis

	Univariate binary logistic regression				Multivariate binary logistic regression			
		95% CI				95% CI		
Variable	OR	Lower	Upper	*P*	OR	Lower	Upper	*P*
ADT	2.885	1.953	4.262	0.001	1.512	1.026	4.786	0.001
Age	0.936	0.618	1.418	0.754	2.847	0.779	7.896	0.441
GS	2.224	1.233	4.014	0.008	1.089	0.298	3.987	0.897
PSA	1.906	1.399	2.597	0.001	1.913	1.759	4.819	0.016
PSAdt	0.817	0.766	0.871	0.001	0.695	0.552	0.873	0.020
PSAvel	1.502	1.297	1.740	0.001	1.028	0.867	1.219	0.753
TNM	1.037	0.519	2.069	0.919	0.654	0.263	1.626	0.361
TTR	1.356	0.879	2.092	0.169	1.595	0.541	4.704	0.397

TTR = time to relapse.

^{11}C-choline PET/CT in the different risk categories are summarized in Figure 2.

Addressing our current study purposes, our results demonstrate that PSA values, PSAdt, and ongoing ADT are the key factors to be considered to select patients who may significantly benefit from restaging ^{11}C-choline PET/CT before S-RT. Therefore, we suggest adding whole-body ^{11}C-choline PET/CT in the diagnostic flow chart of patients with rising PSA values in the early phase of BR and who are eligible for S-RT. The most relevant parameters are PSA $>$ 1 ng/mL or PSAdt $<$ 6 mo or ongoing ADT, because in patients with these characteristics the probability to detect distant additional lesions or locoregional lymph nodes is relatively high.

In a high percentage of patients (72% of the whole population, 433/605 of patients), restaging ^{11}C-choline PET/CT was negative. On one hand, these results stand for a considerably high number of useless ^{11}C-choline PET/CT scans, considering that a negative scan produces no kind of impact on secondary therapy management. On the other hand, as reported by Giovacchini et al. (*30*), a negative scan could be considered as a good prognostic factor on patient survival. In our series, however, a significant proportion of ^{11}C-choline PET/CT–negative patients relapsed during long-term follow-up, confirming that ^{11}C-choline PET/CT has suboptimal sensitivity in the early phase of BR.

This study has some limitations. ^{11}C-choline PET/CT–positive findings were validated mostly by longitudinal follow-up of each lesion after therapy. Histology in each patient would have been preferable but was not feasible because of practical and ethical issues. Other limitations are the lack of data about patient outcome and that the study was based on a retrospective analysis of the data.

TABLE 4
Patient Subpopulations Grouped According to Risk Factors Significantly Related to ^{11}C-Choline PET/CT Positivity and to Prediction of Distant Recurrence Outside Prostate Bed

Population	No. of patients (*n*)	Overall detection rate (%)	Distant relapse (%)	Locoregional LNs (%)
Overall	605	28.4	14.8	8.3
PSA $\geq$ 1.05 ng/mL PSAdt $<$ 5.95 mo*	185	48.6	28.6	9.8
PSA $<$ 1.05 ng/mL PSAdt $\geq$ 5.95 mo*	139	7.9	3.6	2.1
PSA $<$ 1.05 ng/mL PSAdt $\geq$ 5.95 mo Ongoing ADT, no	129	4.6	2.3	1.5
PSA $\geq$ 1.05 ng/mL PSAdt $<$ 5.95 mo Ongoing ADT, yes	68	61.8	36.8	17.6
PSA $<$ 1.05 ng/mL PSAdt $<$ 5.95 mo*	76	44.7	21.1	17.1
PSAdt $\geq$ 5.95 mo*	307	16.4	7.2	3.4
PSAdt $<$ 5.95 mo*	298	47.3	25.9	12.4
PSA $<$ 1.05 ng/mL*	291	23	10	8.5
PSA $\geq$ 1.05 ng/mL*	304	33.4	19.4	8
Ongoing ADT				
No	457	22.7	10.9	6.6
Yes	148	46	26.3	14.2

*All patients in and out of ADT.

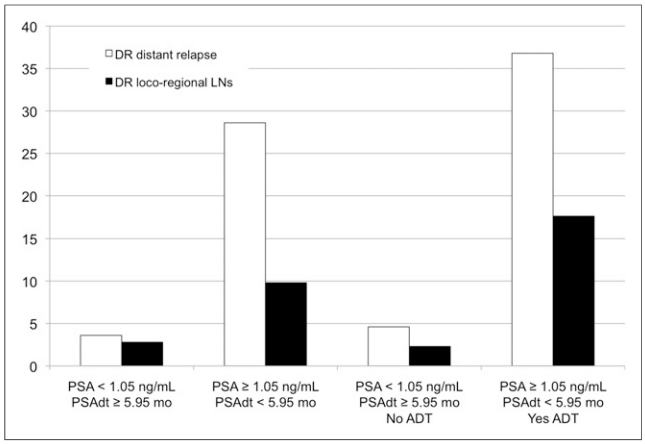

FIGURE 3. ^{11}C-choline PET/CT detection rate in different patient subpopulations.

CONCLUSION

^{11}C-choline PET/CT may be suggested before S-RT during the early phase of BR for the purpose of selecting patients who may significantly benefit from this aggressive treatment. In particular, our results indicate that patients showing fast PSA kinetics and increasing PSA levels despite ongoing ADT should be studied with ^{11}C-choline PET/CT before S-RT because of the significantly high incidence of positive finding outside the pelvis. Further clinical trials, assessing the outcome of patients treated according to ^{11}C-choline PET/CT data, should be performed in the future.

DISCLOSURE

The costs of publication of this article were defrayed in part by the payment of page charges. Therefore, and solely to indicate this fact, this article is hereby marked "advertisement" in accordance with 18 USC section 1734. No potential conflict of interest relevant to this article was reported.

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